Attorney Docket No.: T7106(C)
Serial No.: 10/583,230
Filing Date: June 16, 2006
Confirmation No.: 8226

BRIEF FOR APPELLANT

Sir:

This is a Brief on appellant's Appeal from the Examiner's Rejection in an Office Action mailed April 7, 2010, concerning the above-identified application. The claims in the application have been rejected at least twice.

The Commissioner is hereby authorized to charge any additional fees, which may be required to our deposit account No. 12-1155, including all required fees under: 37 C.F.R. §1.16; 37 C.F.R. §1.17; 37 C.F.R. §1.18.; 37 C.F.R. §1.136.

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I. REAL PARTY IN INTEREST

Conopco, Inc., d/b/a Unilever, a corporation of New York is the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

There are no other prior or pending appeals or interferences or judicial proceedings known to appellant, the appellant's legal representative, or assignee which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

III. STATUS OF CLAIMS

Claims 1, 4, 5 and 7-14 stand rejected in a Office Action mailed January 7, 2010.

Claims 7-12 have been withdrawn

No claims have been allowed.

Claims 2, 3 and 6 have been canceled

Claims 1, 4, 5 and 7-14 are on Appeal.

IV. STATUS OF AMENDMENTS

No claims were amended subsequent to the Office Action mailed January 7, 2010.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The object of the present invention is to provide a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase, with substantially the same pressure at the inlet port of each of the microfluidic units, and stability of the flow to small pressure fluctuations or small differences between the resistance of each of the microfluidic units (page 7, lines 4-11).

Independent claim 1 is directed to a microfluidic system including first and second fluid supply sources (original claim 1, page 7, lines 5-6). The first and second supply sources supply at least 1000 microfluidic reactors (page 10, lines 22-23) arranged in parallel (page 7, lines 4-11, page 15, line 14 page 16, line 7 and Figures 1 and 2) via an upstream channel or channels (page 15, line 24 and Figure 1). The upstream channel or channels positioned before the microfluidics reactors (page 9, lines 4-5). The reactors each have at least one downstream channel which is positioned after the reactors (page 9, lines 7-8). For all the reactors (original claim 6), the resistance of each of its upstream channels is at least 10 times larger than the resistance of the downstream channel or channels (page 9, lines 22-24).

Claim 4 specifies that the resistance of all the upstream channels recited in claim 1 is at least 100 times larger than the resistance of the downstream channels (page 9, line 22-23).

Claim 5 specifies that the microfluidic reactors recited in claim 1 are all identical (page 11, lines 4-6).

Claim 13 specifies that the microfluidic system according to claim 1, comprises at least the following 3 layers (page 12, line 8):

(i) an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel (page 12, lines 9-20);

(ii) a connecting layer comprising a plurality of side channels with varying diameter and/or length (page 12, line 22-32); and

(iii) a microfluidic layer, which comprises microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer (page 13, lines 1-10).

Claim 14 specifies that the system recited in claim 13 comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer (page 14, lines 5-7).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Are claims 1, 4, 5, 13 and 14 enabled under 35 USC 112 first paragraph?

Are claims 1, 4, 5, 13 and 14 indefinite under 35 USC 112, second paragraph?

Are claims 1, 4 and 5 anticipated under 35 USC 102(b) by Anderson et al (US 2003/0053934)?

Are claims 13 and 14 unpatentable under 35 USC 103(a) over Anderson et al (US 2003/0053934)?

Are claim 1, 4 and 5 unpatentable under 35 USC 103(a) over Allen et al (WO 01/128670)?

VII. APPELLANT'S ARGUMENTS

Are claims 1, 4, 5, 13 and 14 enabled under 35 USC 112 first paragraph?

Claim 1

The Examiner asserted that the specification does not provide enablement for *1,000 microfluidic reactors* recited in claim 1. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains to make the invention commensurate in scope with the claims. The Examiner further asserted that the specification is not enabling because it is not clearly stated how 1,000 reactors and channels are being connected.
Appellants respectfully traverse this rejection.

Appellants first disclose that their invention is specifically directed to *a fluid distribution system, allowing to feed several fluid phases to any number of parallel microfluidic units from a single or multiple source for each phase* (page 7, line 4-11).

Appellants disclose on page 10, lines 19-23 that *when used for numbering-up the number of microreactors will generally be from 1000 to 100000 and the number of feeding channels is adapted thereto. For example it could be at least 1000 or even at least 50000.* The term "numbering-up" refers to the use of many parallel devices (page 1, lines 29-30). Thus, one expressly taught aspect of the invention is a network including a large number of micro-reactors. The next question to consider is whether appellants adequately teach *how* such an apparatus can be constructed.

Appellants teach on page 14, line 9 to page 16, line 7 in combination with Figures 1 and 2, two alternative embodiments of a microfluids network that can be scaled up to *any number of reactors*. Specifically, appellants, generalize the essential elements required for any number of reactors on page 15, line 14 to page 16, line 8 which in pertinent states:

The simple microfluidic network presented in Figure 1/2 can be generalized in the following way. A more complex microfluidic network involving the parallel action of at least 2 reactors receiving at least 2 different fluids from at least 2 external sources, with exactly one source per fluid, will require the following elements:

- *(i)* *inlets and outlets for the fluids*
- *(ii)* *"splitting node" splitting the fluids coming from the inlets to the various micro-processing elements.*
- *(iii)* *upstream channels, located between the split and the points where the various fluids meet. These upstream channels are optionally used in the processing, for example for cooling, heating, or otherwise processing the inlet fluids before they join.*
- *(iv)* *joining nodes, where the fluids from the at least two sources meet and start to interact; these joining nodes may be the reactors.*
- (v) *Downstream channels, located after the joining node, respectively after the reactors, and leading to either the outlets or any collecting channel or gutter*

> *which collects the output from the various processing elements. The downstream channels are optionally used to further process the at least two fluids together.*

Appellants' respectfully submit that the above teachings and other teaching found in the specification would have provided adequate guidance to a person of ordinary skill in the relevant art to which the invention pertains (e.g., graduate physical chemist, chemical engineer or physicist with several years of experience in fluids mixing) to design and construct a microfluids system having 1,000 micro-reactors or more.

For example, the artisan could have designed the network simply by starting with the apparatus diagrammed in Figure 1 and the generalized prescription discussed above and given on page 15, line 14 to page 16, line 8, and progressively add splitting nodes to the α and β paths (α1, α2, α3,.....and β1, β2, β3....) each ending at joining nodes which could simply be the inlet of each mico-reactor (1, 2, 3, ...). The skilled person again following the generized plan, would add downstream channel or channels for outflow from each micro-reactor (γ1, γ2, γ3,....pathways) which leads to either the outlets or any collecting channel or gutter which collects the output from the various processing elements.

The artisan could have choosen to either fabricate the device from individual tubes, splitting nodes (e.g. "T" connectors) and micro-reactors (e.g. opposing nozzles) as in Figure 1. However, the specification teaches that a three-layer construction is preferable (page 12, line 8). In this embodiment, appellants suggest that (page 13, lines 13-16) a large number of channels or micro-reactors could be etched on an individual surface much like an integrated circuit board. Appellants submit that such fabrication methods are known in the art, e.g., laser ablation (page 13, lines 15-16).

For example, appellants teach on page 12 , line 8 to page 14, line 7 a microfluidic system that *comprises at least 3 layers*: an inlet/outlet layer comprising inlet channels for the first and second fluid supply sources and at least one outlet channel; a connecting layer comprising a plurality of side channels with varying diameter and/or length; and a microfluidic layer, which comprises the microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer.

The materials and method of fabrication used to construct the layers are also disclosed. Appellants, for example point out that in a preferred embodiment of the invention, the microfluidic layers need only be etched on their surface, which may be made using a variety of *easily accessible microfabrication techniques*, including, but not limited to, wet and dry etching, molding, laser ablation.

Based at least on the above arguments appellants respectfully submit that claims 1, 4, 5, 13 and 14 are fully enabled by the specification.

Are claims 1, 4, 5, 13 and 14 indefinite under 35 USC 112, second paragraph?

<u>Claims 1, 4 and 5</u>

In regard to claims 1 and 4, the Examiner asserted that the recitation of "the resistance of each of its upstream channels is at least 10 times larger (or 100 times larger in claim 4) than the resistance of the downstream channel or channels" renders the claim unclear because it is not specific to the conditions of the fluid, such as temperature, viscosity or flow rate. Appellants' respectfully traverse this rejection.

Appellants' claims are directed to a microfluids system where a first and second supply sources supplies fluids to multiple microfluidic reactors arranged in parallel via an upstream channel or channels. Thus, the two fluids supplied to the upstream channel is the same for all the reactors. Therefore, the temperature, and viscosity of each type of fluid, e.g., the first fluid, is sensibly the same in each reactor. However, this is not necessary as shown by the following analysis.

Appellants' teach on page 2, lines 2-23, especially lines 14-20 that for the simplest case of channels of circular cross section, the resistance R is given by:

$$R=(8*m*L)/(\pi* d^4),$$

where L is the length of the channel and d its diameter.

Thus, for each reactor, the condition that $R_u \geq 0\ R_d$ requires that

$$L_u(d_u^4) \geq 10L_d(d_d^4)$$

where R_u, L_u, and d_u are the resistance, length and diameter of the upstream channel and R_d, L_d and d_d are the resistance, length and diameter of the downstream channel.

Thus, appellants teach that the ratio of resistances of the fluid in channels upstream and downstream to each micro-reactor can be controlled to achieve the resistance limitation recited in claims 1 (or 4) at least by using circular channels and by choosing diameters and lengths for each upstream and downstream channel pair to satisfy the above equation. Since quantitative relationships for non-circular channels are also known from fluid dynamics, similar relationships for channels of non-circular cross section can also be derived.

Based on the above analysis derived from the teachings in appellants' specification, appellants respectfully submit the metes and bounds of claims 1, 4 and 5 are clear and definite.

Claim 13

The Examiner further asserted that in regard to claim 13 it is unclear "how each layer is connected and functions together, in example, are the layers connected horizontally or stacked on each other. It is unclear how the inlet/outlet channels are connected to the reactors".

Applicants respectfully direct the Boards attention to page 12, lines 8 to page 13, line 21 of which the most pertinent sections are:

> Preferably the microfluidic system comprises at least 3 layers. The first layer comprises at least two main inlet channels for fluid supply, and at least 1 outlet channel. This layer is also referred to as inlet/outlet layer. *The inlet and outlet channels are preferably arranged parallel* ......
>
> The connecting layer is preferably positioned *between* the inlet/outlet layer and the microfluidic layer. The connecting layer comprises a plurality of side channels with varying diameter and/or length. This difference in diameter/length enables control over the pressure and flow rate conditions experienced by the microfluidic elements connected to the channels of the connecting layer. ...
>
> The third layer is the microfluidic layer, which comprises a plurality of microfluidic reactors. *These reactors are connected to the*

> *connecting channels via a port* and through the connecting channels they are in fluid connection with the main channels that provide the feeding material. ……
>
> Preferably the at least three layers are connected to each other using conventional techniques such as clamping, bolting, bonding e.g. by high temperature treatment, depending on the material that is used.

Appellants submit that a graduate physical chemist or chemical engineer with several years experience in fluids mixing, i.e., a person of ordinary skill in the art, armed with the above description of a three-layer system and the generalized scale-up description discussed above (with Figures 1 and 2) could have constructed <u>either</u> *a horizontial or stacked apparatus. Both* types of apparatus would be within the scope of the invention and the choice would depend on space requirements and other factors. Furthermore, a technologist with this background and level of experience would have surely understood how to connect inlet/outlet channels to the reactors, i.e., use appropriate couplings such as switch-locks as suggested by appellants (page 13, 26-27).

Appellants further submit, that if time and expense warranted it, the artisan would have recognized that a modular type of 3-layer "cassette" system where the input/output layer, connecting layer and micro-reactor layers are stacked together and fastened would have been advantageous from the standpoint of compact size and minimization to tubing. Furthermore, these types of modular systems are well known in the microfluids art (e.g., stacked multi-well plates).

Based on the above discussion, appellants therefore submit that the metes and bounds of claim 13 are clear and definite.

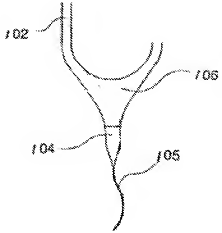
Are claims 1, 4 and 5 anticipated under 35 USC 102(b) by Anderson et al (US 2003/0053934 – hereinafter "Anderson")?

Statement of Facts

Anderson is directed to microfluidic device which comprises two or more microchannel structures (set 1), each of which comprises a structural unit which comprises (i) one or more inlet microconduits, and (ii) an outlet microconduit downstream said one or more inlet microconduits, and (iii) a flow path for a liquid passing through either of said inlet microconduits and said outlet microconduit. *The device is characterized in that each outlet microconduit in said two or more microchannel structures is a* *restriction microconduit* (Abtract – emphasis added).

Anderson specifically teaches that "the structural unit and also the microfluidic device are characterized in that there are means for creating a significant pressure drop in the *outlet microconduits* (105,205,305) (*restriction microconduit*) and possibly also in the microcavities (104,204,304), if present. The flow through the individual microchannel structures, in particular the inventive structural units (as shown in FIG. 1), on a microfluidic device is preferably under common flow control.

FIG 1



105 is an "outlet microconduit (restriction microconduit)" – [0030] and [0042]

104 is a "microcavity" – [0041]

102 is an inlet microconduit - [0041]

In contrast, appellants' microfluids system requires that *for all the reactors, the resistance of each of its upstream channels is at least 10 times larger (100 time larger* in the case of claim 4*) than the resistance of the downstream channel or channels.*

Appellants' Argument

Claims 1, 4 and 5

MPEP 706.02 states "...for anticipation under 35 USC §102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present."

Appellants submit that Anderson does not teach a microfluidics system in which *for all the reactors, the resistance of each of its upstream channels is at least 10 times larger (100 time larger in the case of claim 4) than the resistance of the downstream channel or channels.*

Appellants submit that this limitation is diametrically opposed to the teaching of Anderson. Anderson specifically requires a device characterized in that each outlet microconduit **105** (which correspond to appellants downstream channels defined as channels that are positioned after the two fluid streams meet - page 9, lines 7-8) must be a *restriction microconduit* and thus must have a higher resistance than the inlet microconduit **104** (which corresponds to appellants' upstream channels defined as channels positioned before the fluids meet – page 9, lines 1-4). This is also clear from Anderson FIG 1 in view of the analysis of resistance discussed above.

Appellants submit that absent a disclosure of a microfluidics system in which *for all the reactors, the resistance of each of its upstream channels is at least 10 times larger (100 time larger in the case of claim 4) than the resistance of the downstream channel or channels* Anderson can not anticipate appellants' claims 1, 4 and 5 under 35 USC §102(b).

Are claims 13 and 14 unpatentable under 35 USC 103(a) over Anderson et al (US 2003/0053934)?

Statement of Facts

As discussed above Anderson specifically requires a device characterized in that each outlet microconduit **105** (downstream channel) must be a *restriction microconduit* and thus must have a higher resistance than the inlet microconduit **104** (upstream channels). See Anderson FIG 1 as discussed above.

Anderson is silent about any microfluidics system wherein "for all the reactors, the resistance of each of its upstream channels (i.e.," inlet microconduits") *is at least 10 times larger (100 time larger in the case of claim 4)* than the resistance of the downstream channel or channels (i.e., "outlet microconduits")".

Appellants' Arguments

Claims 13 and 14

To qualify as a 103(a) reference "The prior art reference, or combination of references, must teach or suggest all of the claim limitations (MPEP §2143). In addition to providing at least a suggestion of all the claim limitations, both the suggestion and the reasonable expectation of success must be found in the prior art references, not in Appellant's disclosure" (See In re Vaeck, 20 U.S.PQ.2d 1438, 947 F.2d 448 (Fed Cir. 1991)

Appellants respectfully submit that Anderson does not teach or suggests all the elements recited in claim 13. Specifically, Anderson does not teach or suggest a microfluidics system wherein for all the reactors, the resistance of each of its upstream channels *is at least 10 times larger* than the resistance of the downstream channel or channels.

Appellants respectfully submit that Anderson in fact teaches away from this limitation because Anderson specifically requires a device characterized in that each outlet microconduit **105** (downstream channel) must be a *restriction microconduit* and thus must have a higher resistance than the inlet microconduit **104** (upstream channel) as is evident from Fig. 1 above.

Absent disclosure of a microfluidics system wherein for all the reactors, the resistance of each of its upstream channels *is at least 10 times larger* than the resistance of the downstream channel or channels either explicitly or implicitly and the teaching away from this limitation, Anderson can not present a *prima facie* case of obviousness over claims 13 and 14 at least because these claims incorporate this limitation.

Are claim 1, 4 and 5 unpatentable under 35 USC 103(a) over Allen et al (WO 01/128670 – hereinafter "Allen")?

Statement of Facts

Allen is directed to "a fluidic mixer that mixes two fluids without using mechanical stirrers. The two fluids are fed into an interaction cavity under predeterminable conditions that ensure the fluid flows oscillate and feed in an alternating manner two exit channels. The fluids in the exit channels form interleaved layers having widths related to the frequency of oscillation." (Abstract – emphasis added)

Thus, Allen is concerned with an individual reactor which is designed to osscilate its output stream between two exit channels.

Allen is silent concerning the problem addressed by appellants, namely a microfluidics distribution system that feeds a large number of reactors, e.g., greater than 1000, that is stable to small pressure fluctuations in the distribution channels and shows reduced occurrence of multiphase shunts (page 8, lines 19-21).

Appellants found that "when the resistance of the upstream channel or channels is 10 times higher, preferably 100 times higher than the resistance of the down stream channel or channels, the influence of small variations in flow rate in either of these

channels is limited and hence a more robust system is provided" (page 9, lines 15-20 and 22-4).

Appellants' Arguments

Claims 1, 4 and 5

To qualify as a 103(a) reference "The prior art reference, or combination of references, must teach or suggest all of the claim limitations (MPEP §2143). In addition to providing at least a suggestion of all the claim limitations, both the suggestion and the reasonable expectation of success must be found in the prior art references, not in Appellant's disclosure" (See In re Vaeck, 20 U.S.PQ.2d 1438, 947 F.2d 448 (Fed Cir. 1991)

Appellants respectfully submit that Allen et al does not present a case of *prima facie* obviousness under § 103(a) at least because Allen neither teaches nor suggests the first and second supply sources supplying *at least 1000 microfluidic reactors arranged in parallel* via an upstream channel or channels, said upstream channel or channels positioned before the microfluidics reactors, the reactors each having at least one downstream channel which is positioned after the reactors, wherein for *all the reactors, the resistance of each of its upstream channels is at least 10 (or 100* in the case of claim 4*) times larger than the resistance of the downstream channel or channels.*

Allen is silent about the influence of the relative resistance of liquids in upstream and downstream channels on flow stability in a multi-reator, fluid distribution system when connecting a large number of parallel reactors, let alone that the resistance of *each of its*

upstream channels being at least 10 (or 100) times larger than the resistance of the downstream channel or channels in order to minimize fluctuations and eliminate shunts.

Because it is well known in the art of fluid dynamics that varying cross-sectional dimensions results in varying flow rates, the Examiner asserted that it would have been obvious to one having ordinary skill in the art at the time of the invention to have modified the channel dimensions to increase the resistance of upstream channels at least 10 or 100 times (claim 4) larger than the resistance of the downstream channels *to change the flow rate to modify mixing and reaction rate of fluids*.

However, if the motivation to modify channel dimensions were solely based on the desire *to modify mixing and reaction rate of fluids*, appellants submit that the artisan could equally well have reduced the dimensions of some of the downstream channel (as was done in fact by Anderson discussed above) to achieve an equal or higher resistance in the down stream channels than some or all of the upstream channels. This arrangement is in fact taught by Allen in **Fig 6** where downstream from mixer **612** is channel **616** which serves as *the upstream channel* relative to channels **624**. Since the diameter of channel **624** is smaller than channel **616**, Allen teaches an example where the resistance of a downstream channel (**624)** can be higher than the resistance of its corresponding upstream channel (**616**).

Allen does not deal with a system that involves distribution to a large number of micro-reactors, is silent regarding the problem of instability in such a multi-reactor system, and offers no guidance how this problem should be solved. Allen specifically does not teach or suggest that the relative resistance of flow in upstream Vs downstream channels is a *results-effective variable* as it relates to fluid distribution in a multi-reactor system of the type to which appellants' claims is directed.

MPEP 2144.05B requires that a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

This scale up to 1000 microreactors can not be considered routine on the basis of Allen because Allen does not teach or suggest a key results effective variable that could be used to ensure that flow to such a large number of reactors is uniform and stable.

Appellants respectfully submit that the Examiner has used the knowledge gained from appellants' disclosure as a blueprint to reconstruct their claimed invention from the disclosure of Allen. This approach contravenes the statutory mandate of §103 which requires judging obviousness at the point in time when the invention was made. *Grain Processing v. American Maize-Prods. Co.*, 840 F.2d 902, 907 (Fed. Cir. 1988).

In view of the forgoing arguments, appellants respectfully submit that the claims at issue are fully enabled, clear and definite and are not anticipated or obvious over the

references cited by the Examiner. Appellants respectfully request the Board of Appeals and Interferences to reverse the rejection and have the Examiner issue the claims.

Respectfully submitted,

/ Michael P. Aronson /

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MPA/sm
201-894-2412 or 845-708-0188

VIII. CLAIMS APPENDIX

Claim 1. A microfluidic system comprising first and second fluid supply sources, the first and second supply sources supplying at least 1000 microfluidic reactors arranged in parallel via an upstream channel or channels, said upstream channel or channels positioned before the microfluidics reactors, the reactors each having at least one downstream channel which is positioned after the reactors, wherein for all the reactors, the resistance of each of its upstream channels is at least 10 times larger than the resistance of the downstream channel or channels.

Claim 4. A microfluidic system according to claim 1, wherein the resistance of all the upstream channels is at least 100 times larger than the resistance of the downstream channels.

Claim 5. A microfluidic system according to claim 1, wherein the microfluidic reactors are all identical.

Claim 13. A microfluidic system according to claim 1, wherein the microfluidic system comprises at least the following 3 layers:

(i) an inlet/outlet layer comprising inlet channels for first and second fluid supply source and at least one outlet channel;

(ii) a connecting layer comprising a plurality of side channels with varying diameter and/or length; and

(iii) a microfluidic layer, which comprises microfluidic reactors which are connected to the connecting channels via a port and through the connecting channels are in fluid connection with the inlet and outlet channels of the inlet/outlet layer.

Claim 14. A microfluidic system according to claim 13 wherein the system comprises a plurality of connecting layers connecting a plurality of microfluidic layers to a single inlet/outlet layer.

IX. EVIDENCE APPENDIX

None

X. RELATED PROCEEDINGS APPENDIX

None.